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| EXAMINER | |
|---|---|
| LUCAS, ZACHARIAH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/789,102 | LU ET AL. | |
| | Examiner | Art Unit | |
| | Zachariah Lucas | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *8-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/28/044/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I in the reply filed on May 9, 2005 is acknowledged. The traversal is on the ground(s) that there would be no serious burden in the examination of each of the claimed inventions because each of the inventions includes elements found in the other inventions. This is not found persuasive because while there may be certain elements (i.e. an association of the claimed inventions to the discovery that oncogenic E6 proteins bind to certain PDZ domains), this "common element" does not define each of the claimed inventions or set the limits of the search required therefore. Each of the different methods and compositions claimed requires a different search and search strategy. The Applicant's arguments are therefore not found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 8-22 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 9, 2005.

3. Claims 1-7 are pending and under consideration.

### *Priority*

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an

application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

In the present case, while the application contains reference to the prior applications, the reference does not (generally) include the statement of the relationship of the present application to the prior applications to which priority is being claimed.

5. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> This application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required.
>
> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

The present application is attempting to claim priority to prior U.S. application 09/710,059, filed on November 10, 2000, and abandoned on February 14, 2003. However, the present application

is not copending with the prior application. Additionally, the present application also appears not to be claiming priority to any application which also meets the requirements (reference, copendency, and a common inventor) for priority to this earlier application. The applicant is therefore not accorded benefit to the earlier filing date of the 09/710,059 application.

6. As indicated above, the Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120. The reference to the earlier application indicates above must be submitted during the pendency of the later-filed application. If the later-filed application is an application filed under 35 U.S.C. 111(a), this reference must also be submitted within the later of four months from the actual filing date of the later-filed application or sixteen months from the filing date of the prior-filed application. If the later-filed application is a nonprovisional application which entered the national stage from an international application after compliance with 35 U.S.C. 371, this reference must also be submitted within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371 (b) or (f) in the later-filed international application or sixteen months from the filing date of the prior-filed application. These time periods are not extendable. Except as provided in paragraph (a)(3) of this section, the failure to timely submit the reference required by 35 U.S.C. 120 and paragraph (a)(2)(i) of this section is considered a waiver of any benefit under 35 U.S.C. 120, 121, or 365(c) to such prior-filed application.

A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by

35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional.

### *Information Disclosure Statement*

7. The information disclosure statements (IDS) submitted on July 28, 2004 and on April 21, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

### *Claim Objections*

8. Claim 5 is objected to because of the following informalities: the claim provides the list reading "wherein said candidate agent is small molecule, antibody or peptide." The claim should be amended to introduce the members of the list with an article, and should include a comma between each member (e.g. - - wherein said candidate agent is one of a small molecule, an antibody, or a peptide- -). Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Claim 1 is treated as representative. This claim reads on a method of screening comprising a step of determining the effect of a candidate agent of the binding between and oncogenic E6 protein and the second PDZ domain of the protein MAGI-1. However, the claims do not specify what is being screened for. While the claim indicates that the effect of a compound on E6/MAGI-1 binding is being determined, it is not clear how making such a determination permits a screening. It is suggested that the claims be amended to include a functional statement for the screening (such as screening - - for an inhibitor of oncogenic papillomavirus E6 binding to MAGI-1- -), and a step associating the determining step with the purpose of the screening (e.g., - -wherein a candidate agent determined to reduce binding is a potential inhibitor of E6/MAGI-1 binding- -).

It is further suggested that the claim be amended to more clearly define the method being performed. For example, the Applicant could include steps of providing the oncogenic E6 protein and a polypeptide comprising the second PDZ domain from MAGI-1, and introducing a candidate agent to them.

Clarification of the claims is required.

11. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is treated as representative. The claim reads on a method involving a polypeptide comprising "the amino acid sequence of *a* second PDZ domain from MAGI-1." It is unclear what is meant by reference to a second PDZ domain from MAGI-1. It is not clear how there can be more than one second PDZ domains in a protein. It is therefore suggested that the

claim be amended to read "the second PDZ domain" instead of "a second PDZ domain." Clarification is required.

12. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim further limits claim 1 to a method "further comprising determining the effect of a plurality of candidate agents..." It is not clear from the claim what effect is being determined, or if the determination is being made regarding several candidate agents together, or separately. Clarification is required.

13. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim further limits the methods of claim 1 to embodiments "further comprising testing said agent in a cellular assay for HPV oncogenicity." While it appears that the candidate agent is being tested in an assay for HPV oncogenicity, it is not clear what is being tested for. It is suggested that the claim be amended to indicate that the agent is being tested for the ability to reduce HPF oncogenicity. Clarification is required.

14. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim reads on the method of claim 1, wherein "said determining is a cellular assay." It is not clear what is meant by this claim. It appears that the Applicant intended that the

determining step of claim 1 be performed by way of a cellular assay for E6/ MAGI-1 binding. However, this is not clear from the claim language. Clarification is required.

***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

16. Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Thomas et al. (Thomas I, Oncogene 21: 5088-5096). These claims are directed to method for screening for agents that inhibit binding between the E6 proteins of oncogenic human papillomaviruses (HPV) and the second PDZ domain of the protein MAGI-1. Claim 2 describes the method wherein binding is measured both in the absence and in the presence of the agent. Claim 3 requires the testing of multiple agents. Claim 5 identifies embodiments wherein the agent is one of a peptide, an antibody, or a small molecule. Claim 7 requires the E6 protein and the MAGI-1 peptide are isolated.

Thomas I describes a method for determining if a series of peptides were able to inhibit binding between oncogenic E6 proteins. See, page 5092, right column. The reference teaches that an experiment involving the use of peptides comprising different domains of the MAGI-2 protein to determine which if any of them were able to inhibit MAGI-1/E6 binding (resulting in MAGI-1 degradation). Id, and page 5093, Figure 7(c). The reference also disclosed the use of a control where no additional peptide was added. Thus, the reference meets the limitations of

claims 1-5. The reference teaches that, for the disclosed assay, the E6 and MAGI-1 proteins were translated in vitro. Page 5094 (description of the in vitro degradation assay). Thus, the proteins were not in their natural surroundings, and thereby meet the "isolated" limitation of claim 7. The reference therefore anticipates the indicated claims.

It is noted that the Thomas I reference teaches that the first, rather than the second, PDZ domain of MAGI-1 is bound by the HPV E6 proteins. Page 5090 (section entitled *Homology within the MAGI protein sequences*). However, it is also noted that page 13 of the present application indicates that the section referred to in the present application as the second PDZ domain is not uniformly referred to as such in the art, and that determination as to whether a PDZ domain in the art is the same as in the present application should be based on the sequence. The sequence provided in the application for the second PDZ domain of MAGI-1 encompasses that of the PDZ1 domain described by the Thomas I reference. Cf., SEQ ID NO: 219 (App., Table 8 on page 127) with MAGI-1 PDZ1 sequence disclosed on page 5091 of Thomas I. Thus, while the reference refers to the PDZ1 domain, this domain is the same as that referred to as the second PDZ domain of MAGI-1 in the present application.

It is further noted that the reference has a publication date (August 2002) after the earliest priority date of the present application. However, the earlier applications (esp. PCT/U.S.02/24655, 10/080273, and 09/710,059) do not provide support for the present methods of identifying agents that inhibit binding specifically between MAGI-1 and HPV E6. Thus, the application is not granted priority prior to February 27, 2003 (the filing date of U.S. provisional 60/450,464).

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas I as applied to claims 1-3, 5, and 7 above, and further in view of the teachings of Vidal et al. (Vidal I- Proc Natl Acad Sci 93: 10315-10320) and Vidal et al. (Vidal II- Trends Biotechnol 93: 10315-10320). Claims 1-3, 5, and 7 have been described above. Claim 6 describes the method of claim 1 wherein a cellular assay is used to determine if the candidate agent is able to interfere with binding between the HPV E6 protein and the MAGI-1 PDZ2 polypeptide.

The teachings of Thomas I have also been described above. However, as indicated above the reference teaches an in vitro degradation assay to determine binding between E6 and MAGI-1 PDZ2 in the presence of a candidate agent. The reference does not teach the use of a cellular assay for making such a determination.

However, the Vidal references teach a method of identifying modulators of protein-protein interactions within a cell (the yeast two-hybrid system). The method is a cellular assay involving the detection of expression (or modulation) of a reporter in a cell in the presence of the candidate agent, where the reporter's expression is dependent on the target protein-protein

interaction. See e.g., Vidal I, page 10318. The reference teaches that this method may be applied for the identification of peptides and other therapeutic agents capable of inhibiting target protein-protein interactions. Id., and page 10320. In addition to providing supportive teachings to Vidal I, the Vidal II reference additionally teaches that this cellular method provides several advantages over that of prior biochemical (I.e. non-cellular) methods of identifying such binding inhibitors. Page 375. These references therefore teach the use of a cellular assay for the identification of inhibitors or specific protein-protein interactions as potential therapeutic agents.

Thus, the Thomas I reference teaches that the interaction between oncogenic HPV E6 proteins and PDZ domain 2 of MAGI-1 is a potential target for the treatment of HPV associated cancers, and the Vidal references teach a cellular assay for the identification of inhibitors of such protein interactions. From these teachings, it would have been obvious to one of ordinary skill in the art to have used the cellular assay of Vidal for the identification of inhibitors as suggested by Thomas I. Those in the art would have been motivated to use the method of Vidal as the reference teaches that the cellular assay described therein is superior in certain respects over the biochemical methods otherwise used in the art. Because the Thomas I reference demonstrates that inhibition of E6/MAGI-1 binding reduces the degradation of the MAGI-1 protein, and indicates that such inhibition would decrease the oncogenicity of HPV infection, and because the Vidal references demonstrate that the yeast two-hybrid system is effective for the identification of protein interaction inhibitors, those of ordinary skill in the art would have had a reasonable expectation of success in the combination. The combined teachings of these references therefore render the claimed methods obvious.

19. Claims 1-5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas I as applied to claims 1-3, 5, and 7 above, and further in view of Lorincz et al. (U.S. 6,355,424). Claims 1-3, 5, and 7 have been described above. Claim 4 describes the methods of claim 1, wherein the method further comprises a testing the agent in a cellular assay for HPV oncogenicity. It appears that the Applicant intended to claim a method in which an agent identified as an inhibitor of E6/MAGI-1 binding is further tested in a cellular assay for the ability to inhibit HPV E6 oncogenicity.

The teachings of Thomas I have been described above. The reference teaches a method according to claim 1. Further, the reference also suggests the identification of inhibitors of E6/MAGI-1 binding as potential chemotherapeutic agents. Abstract, and page 5094. Because the reference suggests the identification of inhibitors of E6 and MAGI-1 binding as potential chemotherapeutic agents, it would have been obvious to those in the art to test the agents for the ability to inhibit E6 protein oncogenicity. Such would be a natural step in the identification of chemotherapeutic agents. However, the reference does not teach cellular assays for such testing.

Lorincz teaches assays for the detection of cell states upon HPV infection. Among the methods described by the reference are assays in which cell morphology is followed after HPV infection to determine the progression of the infection, and the development of secondary diseases such as HPV related cancer. See, column 4. The reference further teaches that such assessments may be used not only to determine the state of the HPV infection or HPV-related disorder, but that the assays may also be used for the identification and monitoring of therapeutic regimes. Col. 3, lines 14-20. Thus, the reference teaches a cellular assay for the identification of agents capable of treating HPV-related cancers.

Because the Thomas I reference suggests the identification of agents capable of inhibiting HPV E6 binding to MAGI-1 as potential chemotherapeutic (anti-oncogenic) agents, and Lorincz teaches a cellular assay for the identification of therapeutic treatments for HPV-related cancers, it would have been obvious to those of ordinary skill in the art to use the method of Thomas I to identify inhibitors of E6/MAGI-1 binding, and to further test such agents in the cellular assays of Lorincz for the ability to inhibit HPV oncogenicity. Those of ordinary skill in the art would have had a reasonable expectation of success in the methods based on the indications in the Thomas I reference that inhibitors of E6/MAGI-1 binding were potential source of anti-oncogenic agents, and because the Lorincz reference provides a method of determining if such agents would be capable of inhibiting HPV oncogenicity. The combined teachings of these references therefore render the claimed methods obvious.

20. Claims 1-3, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas II (Oncogene 20: 5431-39), in view of the teachings of Vidal et al. (Vidal I- Proc Natl Acad Sci 93: 10315-10320) and Vidal et al. (Vidal II- Trends Biotechnol 93: 10315-10320). The claims have been described above.

Thomas II provides teachings similar to those of Thomas I with respect to the association between the HPV E6 protein interaction with MAGI-1 and the oncogenic activity of the virus. See esp., page 5437, right column. Further, while the reference does not conduct the assays for binding inhibition disclosed in the Thomas I reference, this reference does suggest the identification of E6/MAGI-1 binding as a target for antiviral and chemotherapeutic activity. Page 3432, first full paragraph; and page 5437, last paragraph before *Material and methods* section.

Thus, these claims therefore provide motivation for those in the art to identify compounds that inhibit this interaction such that these compounds may be further screened for anti-viral and anti-HPV related cancer activity. However, the reference does not teach methods for such identification.

The teachings of the Vidal references have been described above. As indicated above, these references teach methods for identification of inhibitors of target protein-protein interactions. Because the references teach these methods as useful for the identification of such inhibitors, and because the Thomas II reference provides both a suggestion and motivation for the identification of inhibitors of E6 and MAGI-1 interactions, it would have been obvious to those in the art to combine the teachings of these references to as to identify potential anti-HPV agents. The teachings of the references therefore render the claims obvious. Further, those of ordinary skill in the art would have had a reasonable expectation of success based on the information regarding the relationship between the E6/MAGI-1 interaction and HPV-related cancers provides in Thomas. Pages 5431, and 5435-37. In particular, the reference relates the tumor suppressor activity of MAGI-1, and the correspondence between the increased affinity of HPV-18 E6 for MAGI-1 and the higher degree of oncogenicity observed for HPV-18 in caparison to the same traits of HPV-16. Thus, those in the art would have had a reasonable expectation of success in the combination.

It is noted that, like Thomas I, the Thomas II reference also indicates that the affinity for the E6 protein is for the PDZ1 domain, as opposed to the PDZ2 domain as indicated in the rejected claims. However, the reference also teaches that this domain corresponds to a region around residues 454-582 of the MAGI-1 sequence. Page 5438, left column. A comparison of

SEQ ID NO: 219 (identified as the PDZ2 domain of MAGI-1 on page 127 of the application) with that of resides 454-582 of GenPept Accession AAB91995 shows that the two sequences are overlapping. Thus, the PDZ1 domain of Thomas II corresponds to the PDZ2 domain of the present application.

21. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas II (Oncogene 20: 5431-39), in view of the teachings of Bertin et al. (U.S. 6,469,140). The claims have been described above, as have the teachings of the Thomas II reference. While Thomas II suggests the identification of inhibitors of E6/MAGI-1 interactions, the reference does not teach methods of doing so.

However, the Bertin patent does provide such teachings. This reference teaches two unrelated proteins, and means of identifying ligands therefore, and means for identifying inhibitors of binding between those proteins and their ligands. In particular, columns 42-46 provide descriptions of different cellular and non-cellular assays for the identification of compounds that can inhibit the protein-protein interactions of the disclosed protein and their ligands. Further, the reference indicates that such modulators may be identified from chemical groups such as peptides, small molecules and antibodies. Columns 39 and 59. Further, the reference indicates that libraries of such compounds may be screening for the inhibition activity. Column 40. While the reference describes these methods with respect to the disclosed proteins, it would have been clear to those of ordinary skill in the art that such methods could be applied for the identification of inhibitors of any protein-protein interaction. Further, because the reference teaches the screening for compounds that modulate the binding of the compounds, it would have

been apparent that they would have to compare the binding of the protein in the presence of, and in the absence of the compound to determine its effect. Thus, the reference teaches methods of identifying protein-protein interaction inhibitors.

Because the Thomas II reference provides a suggestion and a motivation for the identification of E6/MAGI-1 binding inhibitors, and because the teachings of Bertin illustrate that methods for such detection were known in the art, it would have been obvious to those of ordinary skill in the art to apply the methods described by Bertin to identify inhibitors of E6/MAGI-1 interaction. Those in the art would have had a reasonable expectation of success in the combination based on the teachings of Thomas II (described above), and the teachings in Bertin illustrating the use of these methods for the identification of protein interactions. The teachings of these references therefore render the claimed method obvious.

22. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas II (Oncogene 20: 5431-39), in view of the teachings of Lorincz. The claims have been described above. As indicated above, the Thomas II reference suggests the identification of agents capable of inhibiting binding of E6 and MAGI-1. However, while the reference indicates that such compounds may have chemotherapeutic activity, the reference does not teach a cellular assay for determining if such compounds would inhibit the oncogenic activity of HPV.

However, as described above, the Lorincz reference provides such teachings. See, column 4 (teaching a cell based activity to determine the oncogenicity of HPV); and column 3 (teaching the application of the assays disclosed therein the determine the efficacy of a therapeutic agent or treatment). Because the Thomas II reference suggests the identification of

compounds that inhibit E6/MAGI-1 binding and indicates that such compounds may be useful as chemotherapeutic agents, it would have been obvious to those in the art to test the chemotherapeutic effect of such compounds. As the Lorincz reference provides a cellular assay for making such a determination, it would have been obvious to those in the art to use the assay of Lorincz to determine the effects of the inhibitors identified as suggested by Thomas II on the oncogenicity of HPV, thereby determining their chemotherapeutic potential. Those in the art would have had a reasonable expectation of success in the combination based on the teachings of Thomas II indicating the relationship between such E6/MAGI-1 binding an the virus' oncogenicity, and the teachings of Lorincz indicating the utility of the methods disclosed therein for determining therapeutic effect. The combined teachings of the references therefore render the claimed inventions obvious.

***Double Patenting***

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1-3, and 5-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16, 17, and 19 of copending Application No. 10/847,818. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application read on overlapping subject matter with the present application which overlapping matter renders the present claim obvious.

Claims 1-3 and 5-7 have been described above. Claim 16 of the copending application is drawn to methods of identifying anti-viral agents by screening for inhibitors of PDZ proteins with viral PL (PDZ-ligand containing) proteins. Claims 17 and 19 of the copending application correspond, respectively, to claims 5 and 6 of the present application. Among the PDZ and viral PL proteins sets identified by the application are those of the MAGI-1 PDZ2 and oncogenic HPV E6 proteins. See, page 28, and pages 126-128 (Table 5). The copending application further indicates that the determination required by claim 16 may be performed in the cell-free assays described therein (pages 82), and that the assays for PDZ/PL binding may be conducted both in the presence and absence of the candidate agent (page 83). It is noted that one of the assay forms indicated as useful for the identification of PDZ/PL binding antagonists on page 82 is also described on that page as useful for the screening of libraries of compounds for PDZ binding. Thus, based on these teachings, it would also have been obvious to those in the art that the method of claim 16 of the application could be used to screen a plurality of candidate compounds as potential antagonists. The reference further teaches that the potential antagonists may be from any of a large number of compound groups, including peptide, antibodies, and small molecules.

Page 92. Thus, the copending application renders obvious variants of claim 16 falling within the scope of claims 1-3, 5, and 7.

The application further teaches a cellular (yeast-two hybrid) system for the identification of PDZ interacting proteins. Page 82. Because the reference indicates that such systems may be used both for the identification of PDZ ligands, and antagonists of PDZ/viral PL interactions (Id.), the application also renders obvious variants of claim 16 wherein the determination of candidate agents that reduce PDZ/PL binding is made via a cellular assay. Thus, claim 6 of the present application also represents an obvious variation of the present claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claim 4 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 16 of copending Application No. 10/847,818 in view of Lorincz and Thomas I. As indicated above, claim 4 described embodiments of the claimed invention wherein the method further comprises a step of testing an agent in an assay for HPV oncogenicity. Claim 16 of the copending application is silent as to this additional testing of the compounds identified therein.

However, the reference does indicate that among the targets for anti-HPV agents identified according to the claim is the interaction of oncogenic HPV E6 proteins and the second PDZ domain of MAGI-1. Page 125. The Lorincz reference, as described above, teaches a cellular assay to determine a compounds effect of HPV oncogenicity, but provides no motivation to

apply such a test to a compound inhibiting HPV E6 interaction with a PDZ protein as identified by claim 16 of the copending application.

The Thomas I reference, as indicated above, teaches that the E6/MAGI-1 protein interaction is a target for anti-HPV related cancer therapy. Thus, the teachings of Thomas I provide motivation for those of ordinary skill in the art to further test compounds identified by claim 16 in the cellular assay for HPV oncogenicity described by Lorincz. The combined teachings of these references therefore render the claimed inventions obvious.

This is a provisional obviousness-type double patenting rejection.

26. The above rejections are, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804 II(B)(1):

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is

based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

***Conclusion***

27. No claims are allowed.

28. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> The following references provide examples of teachings related to the screening of compounds for therapeutic activity. Among the general groups of compounds identified are small molecules, peptides, and antibodies. Thus, while adding little specifically relating to the claimed inventions over the teachings of the Thomas I reference, they indicate that screening candidate agents from the groups of molecules listed in claim 5 would have been obvious to those of ordinary skill in the art. Chen et al., U.S. 6,200,780, esp. columns 38-39; and Eckert et al., U.S. 6,818,740, column 2.
>
> Erickson et al., U.S. 5,525,490. The teachings of this reference are considered redundant to those of the Vidal references applied above.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

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